deformities in severe cases. Simultaneously, there is generation of more oxidative stress biomarkers such as Reactive Oxygen species (ROS) and Malondialdehyde (MDA), which is the major reactive aldehyde produced due to peroxidation of lipids present in biological membranes.
We, therefore, investigated the status of oxidative stress quantified in terms of MDA and ROS in serum and lymphocytes, respectively, in patients of OA of knee and correlated the levels of biomarkers with different radiological grades of the disease.
Methods: After obtaining ethical clearance 80 patients, who were suffering from OA of knee were enrolled according to the inclusion / exclusion criteria described by 'The American College of Rheumatology'. Informed consent was taken from all patients and blood samples along with the radiographs of the knee joints were obtained. These patients were subdivided into four groups according to severity of the disease using Kellgren-Lawrence (KL) grading scale and were also analysed for assessment of pain by using Visual Analogue Scale (VAS).
The blood samples were processed to get serum for estimation of MDA using thiobarbituric acid reactive substances assay. For ROS measurement, lymphocytes were isolated from the blood sample using density gradient histopaque solution. These lymphocytes were incubated with 2, 7-dichlorofluorescein diacetate (DCF-DA) dye for 30 minutes and then acquisition was done on Image Stream X Mark II flow cytometer (AMNIS Corporation, Seattle) and analysis was done using IDEAS analysis software.
Results: We found that the levels of both ROS and MDA in KL-grade III and IV patients were significantly higher ($p<0.05$) as compared to the levels of these biomarkers in KL-grade I and II. Further, it was also observed that although the level of both biomarkers was more in KL-grade IV than in KL-grade III but the difference was not significant. The VAS score was found to be highest in KL-grade IV patients as compared to the other three groups.
Conclusions: The study indicates that progression of OA of knee generates more ROS and causes more lipid peroxidation, thus exhibiting more oxidative stress in patients. Hence, it may be proposed that the levels of ROS and MDA are well correlated with progression of OA of knee.

105
THE LOWER CARTILAGE SYNTHESIS, BUT NOT HIGHER CARTILAGE DESTRUCTION, IS ASSOCIATED WITH THE KNEE JOINT SPACE WIDTH IN MEN IN EARLY FORTIES WITHOUT KNEE PAIN

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Purpose: The prevalence of knee osteoarthritis (OA) is peaked at around fifty years of age in worldwide (Global Burden of the Disease 2010). However, it has been recently considered that the knee OA is initiated much younger than fifty years of age and proceeded asymptomatically for a long time. As OA is primarily an age-related degenerative disease of articular cartilage, the radiographic joint space width (JSW) is gradually narrowed and the OA incidence is defined by the joint space narrowing. However, it is poorly understood how the asymptomatic phase of primary knee OA is proceeded. Several cartilage biomarkers have cultivated as a sensitive diagnostic tool for knee OA. Pro-collagen type II C-propeptide (PIICP) is a major articular cartilage constituent and reflects the rate of type II procollagen synthesis. The collagen type II cleavage (C2C) and cross-inked type II collagen C-telopeptide (CTX-II) are produced in the course of degradation of type II collagen. It has been believed that knee OA is primarily characterized by cartilage degradation. We previously reported that the these biomarkers in the primary knee OA patients (K/L grade 1 and 2) with knee pain were all significantly increased in comparison to those without knee pain. In K/L grade 1 patients both sC2C and sCPII were increased in those with knee pain. However, among the K/L grade 2 patients, only uCTX-II was increased and in those with knee pain. In addition, sCPII levels of K/L grade 1 patients without knee pain was decreased in those of K/L grade 2 patients without knee pain, while no significant changes of the sC2C and uCTX-II levels were observed in between K/L grade 1 and 2. In the present study, we examined the interrelationships between the cartilage metabolism and the knee articular cartilage thickness of the healthy subjects at around forty years of age without knee pain using biomarkers.
Methods: Sixty-three healthy men volunteers (41.7y in average) were enrolled in this study. The subjects didn't have any symptoms for knee pain and experience any traumatic episodes for their knee joints. The standing, extended antero-posterior view and the postero-anterior weight-bearing radiograph made with the knee in 45° of flexion (Rosenberg radiograph) were taken for both knees and serum levels of PIICP and C2C and urinary level of CTX-II were also measured at the time of study entry. These cartilage biomarkers were measured by ELISA (PIICP; Uscn life science, C2C IBEX, CTX-II; ids). The JSW of the knee joint was determined at the center point of the medial femoro-tibial compartment on a radiograph using a 0.1-mm graduated magnifying lens. For each participant, the higher K/L grade and the lower JSW of the findings of both knees used for the analysis as targeted knee. The statistical analyses were conducted using the SPSS (SPSS version 17.0). The correlation between every particular objects were assessed by Spearman's rank-correlation coefficient. Relationship between JSW and several targeted cartilage biomarker were assessed by single correlation analysis with adjustment for age and body mass index (BMI). Furthermore in order to find out which cartilage biomarker may be most influent to JSW, relationships between JSW and all targeted cartilage biomarkers were assessed by multiple linear regression analysis (Step Wise) with adjustments for age and BMI.
Results: Of 63 subjects, seventeen, thirty-nine and seven showed the K/L grade 0, 1 and 2 on radiographs, respectively. The serum average level of PIICPs was 327.44 pg/mL (SD; 239.37), the serum average level of C2Cs was 82.51 μg/mL (18.05), the urinary average level of CTX-II was 316.53 ng/mmol (290.51) and the JSW in the targeted knee was 4.65 mm on average (0.96). The JSW was normally distributed. The sC2C and sPIICP were positively correlated ($\beta=0.336$, $p=0.022$), while sC2C and uCTX-II ($\beta=0.010$, $p=0.953$) and uCTX-II and sPIICP were not correlated ($\beta=-0.081$, $p=0.619$). The JSW was positively correlated with both sPIICP ($\beta=0.348$, $p=0.011$) and sC2C ($\beta=0.333$, $p=0.011$), respectively, while no correlation between the JSW and uCTX-II was observed ($\beta=-0.0239$, $p=0.123$). The multiple linear regression analysis showed that sPIICP was the factor that positively correlated with the JSW ($\beta=0.474$, $p=0.001$).
Conclusions: We demonstrated that both cartilage synthesis marker (PIICP) and degradation marker (C2C) are associated with the JSW of the asymptomatic knee of the healthy subjects at around forty years of age. We also demonstrated that the lower cartilage synthesis was most strongly associated with JSW in men in early forties.

106
CARTILAGE OLIGOMERIC MATRIX PROTEIN (COMP) LEVELS IN SERUM AND SYNOVIAL FLUID IN OSTEOARTHRITIS (OA) PATIENTS: CORRELATION WITH CLINICAL, RADIOLOGICAL AND LABORATORY PARAMETERS

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Purpose: The aim of the study is to assess the cartilage oligomeric matrix protein (COMP) levels in serum and synovial fluid in osteoarthritis (OA) patients and to correlate the levels with clinical, radiological and laboratory parameters.
Methods: 23 OA patients were included. Thorough history taking and clinical examination were performed. Serum and synovial COMP were determined by ELISA. Osteoarthritis severity was assessed according to the Kellgren-Lawrence (KL) scale. Patients were subgrouped into early and late OA according to the presence of knee destruction (grades $\geq$3 KL scale).
Results: The mean age of the patients was 45±12.9 years. 9 had concomitant knee effusion. The KL scale was significantly higher in patients with established (3.4±0.5) compared to those with early OA (1.7±0.5). The serum COMP was significantly higher in the OA patients (27±10 μg/ml) compared to the control (5.4±2μg/ml) ($p<0.00001$). In synovial fluid it was even higher (59.1±11.4μg/ml). Serum and synovial levels were higher in established compared to early cases. Serum and synovial levels significantly correlated with the age, body mass index, disease duration and KL grade.
Conclusions: Assay of COMP in serum/synovial fluid could mirror the process of articular damage in OA patients. Promisingly, COMP levels have the potential to be reliable diagnostic markers in the assessment of early joint destruction in and can guide to predict the disease outcome for rapid treatment initiation in patients at early stages. Levels correlated with radiological joint damage but not with clinical disease parameters, thus can be used for monitoring the response to different therapeutic modalities.